We thank Dr. Kawada for his interest in our article. He raised 2 important issues: (1) subjects without cardiovascular disease (CVD) also presented no strong association between excessive daytime sleepiness (EDS) and sleep apnea hypopnea index (AHI) and (2) the relationship between SDB and EDS would be diluted in groups without predominant obesity.

EDS is associated with SDB in the general population or sleep clinic patients, but is not invariably present in subjects with SDB. The possible mechanism of the development of EDS in SDB patients could include nocturnal hypoxia, repeated arousals from sleep, or enhanced sympathetic tone, but some results are inconsistent regarding the relationship between EDS and AHI, respiratory disturbance index, or other variable SDB-related parameters.

For instance, a higher respiratory disturbance index was associated with higher prevalence of EDS in community-dwelling, middle-aged and older adults participating in the Sleep Heart Health Study. Subjects participated in several retrospective cohorts including severe adult obstructive sleep apnea patients who underwent polysomnographic evaluation in a sleep disorders unit. In contrast, among 40 patients in a Spanish cohort from the respiratory department of a single university hospital, worse nocturnal oxygenation, but not AHI or the architecture of sleep phases, discriminated between patients with and without EDS. According to reports regarding autonomic arousal during sleep, EDS is associated with a higher low-to-high frequency power ratio of heart rate variability during nocturnal sleep, an indirect index of sympato-vagal balance over the whole night, while no difference in AHI is found between patients with and without EDS. These inconsistent results could be caused by differences in diagnostic methods, EDS or SDB severity, and the demographic characteristics of each cohort. Thus, although EDS is a well-recognized symptom in SDB patients without CVD, the SDB-related parameters that are strongly associated with EDS are still not well understood.

Obesity is known to be linked to EDS and body mass index (BMI) was a significant risk factor for EDS in a cross-sectional study. From a random, general population sample of 1,741 individuals from a sleep laboratory, obesity was a major risk factor for the incidence and chronicity of EDS, while weight loss was associated with its remission. In the Sleep Heart Health Study, weight gain was associated with EDS, mostly through pathways other than SDB. The reasons for the associations are not clear, although SDB and non-SDB factors (e.g., release of proinflammatory cytokines) could contribute to the development of EDS in obese patients; the underlying mechanism is multifactorial. However, in our cohort, obesity, defined as BMI > 25, was not a determinant of EDS, which might be unique to Japan, which does not have an obesity epidemic. Thus, whether our findings can be applied to other countries, especially obesity epidemic areas, remains unknown. Several previous studies demonstrated that the relationship between SDB and EDS was modified by patient characteristics, such as age, sex, and severity of SDB. On the other hand, according to the Sleep Heart Health Study, age, sex, and BMI do not modify this association. Whether the relationship between SDB and EDS is modified by patient background, including obesity, is still not conclusive, and further studies will be needed in the future.

References

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